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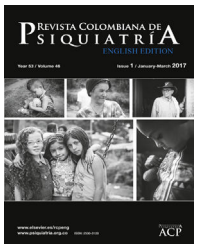

Case Report

Reversible alopecia secondary to OROS methylphenidate☆

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ABSTRACT

Introduction: Attention deficit hyperactivity disorder has a prevalence of 1–4% of the Spanish school population. Its treatment consists of giving amphetamine derivatives and, recently, non-stimulant drugs, without finding any differences in efficacy in the studies performed.
Clinical case: A 7-year-old girl was referred from neurology due to learning delay and behaviour disorders. Diagnosed as likely ADHD, treatment was started with immediate release methylphenidate, and later with an osmotic release oral system (OROS) methylphenidate. When alopecia areata appeared, this treatment was withdrawn. After the re-introduction of modified release methylphenidate 30:70, symptom control was achieved without the appearance of alopecia.
Discussion: There is a published history of two cases of alopecia areata with OROS methylphenidate that resolved after increasing the dose of the drug without clearly knowing the reason for this event. There is no consensus on the priority use of the immediate release formula or the OROS methylphenidate.

Alopecia reversible secundaria a metilfenidato OROS

Palabras clave:
Metilfenidato OROS
Alopecia areata
Efectos secundarios
TDAH

RESUMEN

Introducción: El TDAH tiene una prevalencia del 1–4% de la población escolar española. Su tratamiento se realiza con derivados anfetamínicos y, recientemente, con fármacos no estimulantes; los estudios realizados no han encontrado diferencias de eficacia.
Caso clínico: Niña de 7 años llegó derivada desde neurología por retraso en el aprendizaje y trastornos de conducta. Orientada como TDAH, se inició tratamiento con metilfenidato de

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liberación inmediata y posteriormente con la fórmula OROS; apareció alopecia areata y se retiró el tratamiento. Tras la reintroducción de metilfenidato de liberación modificada 30:70, se consiguió controlar los síntomas sin que apariciera alopecia.

Discusión: Hay antecedentes publicados de 2 casos de alopecia areata con metilfenidato OROS, que se resolvieron tras el aumento de dosis del fármaco, aunque no se conoce claramente el motivo de este suceso. No hay consenso sobre el uso prioritario de la fórmula de liberación inmediata o la fórmula OROS del metilfenidato.

Introduction

Attention-deficit hyperactivity disorder (ADHD) presents in up to 10% of the global population; in Spain, it is detected in 1–4% of the school population.[1] Other studies have determined an estimated prevalence of 5.29%, with no differences between Europe and North America; geographic variability has been explained by methodological characteristics of studies.[2]

Drug treatment for ADHD consists of amphetamine derivatives and, as of recently, non-stimulant drugs. Learning abilities have improved following 12 weeks of treatment with osmotic-controlled release oral delivery system (OROS) methylphenidate, but inhibition has not.[3] Various studies that have evaluated atomoxetine and OROS methylphenidate have not managed to find any differences on traditional rating scales or measures of cognitive function[4] following these treatments.

The most significant adverse effects of methylphenidate include insomnia, headache, tic exacerbation, nervousness, irritability, overstimulation, tremor and dizziness. The peripheral increase in norepinephrine may cause side effects such as tremor, tachycardia, hypertension and cardiac arrhythmias. This increase, along with the increase in dopamine, in the central system may cause insomnia, agitation, psychosis and substance abuse.[5]

Methylphenidate is a drug that has also been used for other psychiatric disorders such as trichotillomania, and has demonstrated certain efficacy in cases with a low rate of stressful life events.[6]

Case report

A 7-year-old girl was referred to a Child and Youth Mental Health Unit from Paediatric Neurology due to developmental delay and behaviour disorders when with her family and at school.

Family history

Her mother was a carrier of hepatitis B, her paternal grandmother had a diagnosis of anxiety–depressive disorder and a paternal cousin had been diagnosed with ADHD.

Personal history

The girl was born prematurely after 34 weeks of gestation; her birth weight was 2.700 kg. There was no evidence of any abnormalities in her psychomotor or language development. She had proper sphincter control at the age of 24 months, with secondary nocturnal and diurnal enuresis. She used a bottle until she was 24 months old and a dummy until she was 5 years old. Her medical and surgical history included planned surgery at age 8 for ankyloglossia, which caused pronunciation difficulties.

Schooling

She started attending school at the age of three, but did not complete the first cycle of early childhood education. She then changed schools multiple times. She was evaluated by a school guidance team and found to have a low-to-medium intellectual capacity, as well as a level of visual perceptual maturity two years behind her chronological age. She received timely educational measures at her school. She was reported to have difficulty integrating into peer groups due to limited social skills and impulsive behaviour.

Family unit

Her parents separated when she was five years old; gender violence was reported as a cause of their separation. Her father, with whom she was in regular contact, lived in another municipality. She lived with her mother, her mother's partner and a sister five years her senior.

Current illness

Starting in early childhood, she showed a persistent pattern of hyperactivity with difficulty focusing on a task, restlessness and excessive movement, maladjusted and hetero-aggressive behaviours of an impulsive nature, limited ability to wait her turn and to think through the consequences of her behaviour, learning difficulties that had been obvious since she started school, difficulty training her attention on activities that required sustained mental effort, distractibility, and little capacity for organisation. She had sleep disorders with conciliation insomnia, as well as abnormal sphincter control with diurnal and nocturnal enuresis, limited autonomy in basic activities of daily living and negativistic and oppositional behaviours, with difficulties following rules and respecting boundaries which were more accentuated when she was with her family. All this resulted in very significant functional limitations which affected her school performance as well as her relationships with her family members and other people, with high levels of stress and frustration. Physical examination revealed a phenotype characterised by brachycephaly and clinodactyly.

Clinical course and treatment

Complementary testing was performed, consisting of a complete blood count, clinical chemistry, ammonium lactate detection, electroencephalogram, computed tomography without contrast and karyotyping. The latter indicated that the patient had fragile X syndrome; all other findings were not significant. A multimodal therapeutic approach was started that included contact and coordination with the girl's school; psychotherapy promoting self-control, autonomy, social skills and conflict resolution strategies; and family psychoeducation towards adoption of more functional parenting styles. Drug treatment was started initially with methylphenidate in immediate-release tablets (10 mg/day). This achieved a significant improvement with respect to her lack of focus, which had favourable repercussions for her academic performance. Her impulse control improved, her behaviour disorders remitted and she was able to better integrate into a group of peers.

After three months, her treatment was replaced with OROS methylphenidate 18 mg/day tablets. Her response was excellent, and she remained asymptomatic with normalised general functioning.

After four months had elapsed since her treatment was readjusted, she required urgent care due to multiple alopecia plaques on her scalp, eyebrows and eyelashes. Her treatment with methylphenidate was suspended, whereupon her hair stopped falling out and regrew in the affected areas. Her treatment remained suspended for three months and her alopecia completely resolved. However, she redeveloped a persistent pattern of lack of focus, hyperactivity and impulsivity which very significantly interfered with her general functioning; therefore, both the girl and her mother requested that her methylphenidate treatment be restarted, given the girl's excellent prior response.

Following failure of other therapeutic measures, immediate-release methylphenidate, which had previously been well tolerated, was restarted, although the dose had to be increased to 20 mg/day. After two months of treatment with a good clinical response, the alopecia plaques reappeared and the drug had to be suspended.

Following four months without treatment and another instance of clinical decompensation, immediate- and extended-release methylphenidate (modified-release capsules) 30:70 was started. With this, the patient remained stabilised and experienced no significant adverse effects.

Discussion

A recently published case report described the development of alopecia areata plaques in two patients who were siblings two weeks after they started treatment with OROS methylphenidate. These plaques resolved when the drug was reintroduced and the dose was increased.[7]

Other better known side effects associated with the use of methylphenidate are poor appetite, sleep difficulties, epilepsy, tics, palpitations and other dermatological problems such as cold extremities, diaphoresis, rashes and acne.[8]

Regarding the possibility of using methylphenidate with different forms of release — immediate release, modified release or the OROS form — it has been observed that short release is preferred by school personnel and extended release is preferred by parents of children and adolescents with ADHD.[9] No differences in adverse effects between the different forms of presentation have been detected.

In this case report, alopecia areata developed as a side effect after OROS methylphenidate was started. Although this side effect is among the side effects of methylphenidate that have been reported, in some cases, alopecia resolves once the drug dose is increased.

Further studies of this event must be conducted to arrive at a more satisfactory and objective explanation thereof and to identify or rule out a relationship between the onset of alopecia areata and the concentration of this drug. Recent studies have raised the possibility of monitoring methylphenidate and/or its metabolite in the saliva, sweat or hair as non-invasive testing techniques.[1]

Conflicts of interest

None.

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